REMARKS

The Present Invention

The present invention is directed to compounds comprising the Dmt-Tic pharmacophore, related compositions and methods of use.

The Pending Claims

Claims 1, 10, 11 and 15-24 are pending. Claims 1, 19 and 21-23 are directed to compounds, whereas claims 10, 20 and 24 are directed to the compositions comprising such compounds, and claims 11 and 15-18 are directed to methods of use.

The Amendments to the Claims

Claim 1 has been amended to point out more particularly and claim more distinctly the present invention. In particular, claim 1 has been amended to recite certain moieties for R''. Applicants thank Examiner Lukton for the telephonic interview with Applicants' representative, Kristen J. Harrell, on July 14, 2003, during which the language of claim 11 was discussed. Claim 11 has been amended in accordance with the Office's suggestion solely in an effort to advance prosecution and not in acquiescence of the Office's rejection for the reasons set forth herein. In particular, claim 11 has been amended to recite a method of antagonizing a δ-opioid receptor in a mammal in need thereof with at least one compound of the present invention, as supported by the specification at, for example, page 17, line 11, through page 19, line 1. No new matter has been added by way of this amendment.

The Office Action

Claim 11 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Claims 1, 10 and 15-24 have been allowed. Reconsideration of the pending claims is hereby requested.

Discussion of the Rejection Under 35 U.S.C. § 112, first paragraph

The Office has rejected claim 11 under Section 112, first paragraph, as allegedly lacking enablement. Specifically, the Office contends that the specification does not provide evidence that the compounds of claim 11 have a therapeutic effect, such as providing analgesia. However, the Office states that "[a]s for the 'state of the art', there are examples of compounds which are effective to antagonize the *delta*-opioid receptor *in vitro*, and which also induce analgesia" (Office Action, page 3, first full paragraph). In making such a statement, the Office acknowledges that the state of the art is such that one of ordinary skill in the art would

reasonably believe that a compound that antagonizes the *delta*-opioid receptor *in vitro* also induces analgesia. In other words, compounds that antagonize the *delta*-opioid receptor *in vitro* have therapeutic efficacy *in vivo*. This, coupled with the teachings of the instant specification can only lead one to conclude that the instant specification is, in fact, enabling for a method of treating a mammal as claimed in claim 11.

In order for an invention to be considered enabled, Applicants need only teach those of ordinary skill in the art how to make and use the present invention. In this regard, Applicants point out that Example 47 of the instant specification describes the *in vitro* efficacy of the compounds of claim 11 in binding to the δ-opioid receptor. Conditions which might be treated by such antagonism, described in the specification at, for example, page 17, line 11, through page 19, line 8, and page 23, lines 9-14. Chemical synthesis of the compounds recited in claim 11 is described in the specification at, for example, the Example section, such as Example 40. Suitable doses are described in the specification at, for example, page 23, line 15, to page 24, line 33. Formulations are described in the specification at, for example, page 15, line 23, to page 17, line 5, and includes modes of administration, carriers, and excipients. Therefore, no undue experimentation would be required for one of ordinary skill in the art to practice the method of claim 11, and the state of the art provides a reasonable expectation of success.

While the Office cites various literature references in a final effort to contend that *in vitro* results do not always provide *in vivo* efficacy, and that, therefore, claim 11 is not enabled, Applicants point out that several of the cited references relate to completely different methods (e.g., stimulation of growth hormones, cAMP production in cells, and inhibition of the MSH receptor relating to melanogenesis) and all of the references relate to compounds that are structurally different from those recited in claim 11. Moreover, it should be noted that the cited references do *not* indicate that *in vitro* potency is not indicative of *in vivo* efficacy. Instead, the references indicate that increased *in vitro* binding affinity did not always *correlate* with increased *in vivo* efficacy. This does not constitute a teaching that such compounds are necessarily without therapeutic effect. Rather, this merely suggests that such compounds may not be ideal candidates for therapy. In this regard, Applicants point out that even the instant specification teaches that conventional techniques, such as the tail flick test described in the instant specification at page 15, lines 14-22, are routinely used to determine *in vivo* efficacy.

Accordingly, Applicants adamantly maintain that claim 11 is enabled by the specification for a method of treating a mammal in need thereof. However, in an effort to advance prosecution, claim 11 has been amended as indicated above. Applicants maintain

the right to pursue method of treatment claims in subsequent applications. In view of the foregoing, the rejection should be withdrawn

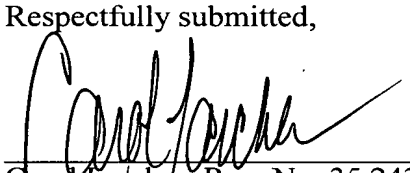
Drawing

Applicants request that the U.S. Patent and Trademark Office indicate the acceptability of the drawing filed with the present application. To date, the acceptability (or lack thereof) of the drawing has not been received.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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